

Please **add** new claims 39-86.

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39. (NEW) A nucleic acid comprising a nucleic acid sequence which encodes the carboxy-terminal portion of the heavy chain of a botulinum neurotoxin serotype selected from the group consisting of serotype B, serotype C<sub>1</sub>, serotype D, serotype E, serotype F, and serotype G and is capable of being expressed in an organism selected from the group consisting of a gram negative bacteria, a yeast, and a mammalian cell line.
40. (NEW) The nucleic acid of claim 39, wherein the gram negative bacteria is *Escherichia coli*.
41. (NEW) The nucleic acid of claim 39, wherein the yeast is *Pichia pastoris*.
42. (NEW) The nucleic acid of claim 39, wherein said nucleic acid comprises a nucleic acid sequence selected from the group consisting of SEQ ID No. 7, SEQ ID No. 9, SEQ ID No. 11, SEQ ID No. 13, SEQ ID No. 15, and SEQ ID No. 17.
43. (NEW) A nucleic acid comprising a sequence which encodes a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12, SEQ ID No. 14, SEQ ID No. 16, and SEQ ID No. 18.
44. (NEW) The nucleic acid of claim 39, wherein said nucleic acid is a synthetic nucleic acid.

45. (NEW) The nucleic acid of claim 39, wherein said nucleic acid is operably linked to expression control sequences.
46. (NEW) The nucleic acid of claim 39, wherein said expression control sequences comprise a promoter.
47. (NEW) The nucleic acid of claim 39, wherein said expression control sequences comprise an enhancer.
48. (NEW) A method of preparing a polypeptide comprising the carboxy-terminal portion of the heavy chain of a botulinum neurotoxin serotype selected from the group consisting of serotype B, serotype C<sub>1</sub>, serotype D, serotype E, serotype F, and serotype G, said method comprising
- transfecting an organism with the nucleic acid of claim 39;
- culturing the transfected organism under conditions wherein the carboxy-terminal portion of the heavy chain of a botulinum neurotoxin serotype is expressed, wherein the organism selected from the group consisting of a gram negative bacteria, a yeast, and a mammalian cell line.
49. (NEW) The method of claim 48, further comprising recovering insoluble protein from said transfected organism.
50. (NEW) The method of claim 48, wherein said organism is *Escherichia coli*.
51. (NEW) The method of claim 48, wherein said organism is *Pichia pastoris*.

52. (NEW) An immunogenic composition comprising the carboxy-terminal portion of the heavy chain of a botulinum neurotoxin serotype selected from the group consisting of serotype B, serotype C<sub>1</sub>, serotype D, serotype E, serotype F, and serotype G.
53. (NEW) A method of preparing the immunogenic composition of claim 52, said method comprising culturing a recombinant host organism transfected with an expression vector encoding, in an expressible form, the carboxy-terminal portion of the heavy chain of a botulinum neurotoxin serotype.
54. (NEW) A method of preparing the immunogenic composition of claim 52 comprising culturing a recombinant organism capable of expressing the carboxy-terminal portion of the heavy chain of a botulinum neurotoxin serotype and recovering an insoluble protein fraction from the recombinant organism.
55. (New) The nucleic acid of claim 39, wherein the A+T content is less than about 70% of the total base composition.
56. (New) The nucleic acid of claim 55, wherein the A+T content is less than about 60% of the total base composition.
57. (NEW) A nucleic acid comprising a nucleic acid sequence which encodes the amino-terminal portion of the heavy chain of a botulinum neurotoxin serotype selected from the group consisting of serotype B, serotype C<sub>1</sub>, serotype D, serotype E, serotype F, and serotype G and is capable of being expressed in an organism selected from the group consisting of a gram negative bacteria, a yeast, and a mammalian cell line.

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58. (NEW) The nucleic acid of claim 57, wherein the gram negative bacteria is *Escherichia coli*.
59. (NEW) The nucleic acid of claim 57, wherein the yeast is *Pichia pastoris*.
60. (NEW) The nucleic acid of claim 57, wherein said nucleic acid comprises a nucleic acid sequence selected from the group consisting of SEQ ID No. 21, SEQ ID No. 23, SEQ ID No. 25, SEQ ID No. 27, SEQ ID No. 29, and SEQ ID No. 31.
61. (NEW) A nucleic acid comprising a sequence which encodes a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID No. 22, SEQ ID No. 24, SEQ ID No. 26, SEQ ID No. 28, SEQ ID No. 30, and SEQ ID No. 32.
62. (NEW) The nucleic acid of claim 57, wherein said nucleic acid is a synthetic nucleic acid.
63. (NEW) The nucleic acid of claim 57, wherein said nucleic acid is operably linked to expression control sequences.
64. (NEW) The nucleic acid of claim 57, wherein said expression control sequences comprise a promoter.
65. (NEW) The nucleic acid of claim 57, wherein said expression control sequences comprise an enhancer.
66. (New) The nucleic acid of claim 57, wherein the A+T content is less than about 70% of the total base composition.

67. (New) The nucleic acid of claim 66, wherein the A+T content is less than about 60% of the total base composition.
68. (NEW) A method of preparing a polypeptide comprising the amino-terminal portion of the heavy chain of a botulinum neurotoxin serotype selected from the group consisting of serotype B, serotype C<sub>1</sub>, serotype D, serotype E, serotype F, and serotype G, said method comprising
- transfecting an organism with the nucleic acid of claim 57,
- culturing the transfected organism under conditions wherein the amino-terminal portion of the heavy chain of a botulinum neurotoxin serotype is expressed, wherein the organism selected from the group consisting of a gram negative bacteria, a yeast, and a mammalian cell line.
69. (NEW) The method of claim 68, further comprising recovering insoluble protein from said transfected organism.
70. (NEW) The method of claim 68, wherein said organism is *Escherichia coli*.
71. (NEW) The method of claim 68, wherein said organism is *Pichia pastoris*.
72. (NEW) An immunogenic composition comprising the amino-terminal portion of the heavy chain of a botulinum neurotoxin serotype selected from the group consisting of serotype B, serotype C<sub>1</sub>, serotype D, serotype E, serotype F, and serotype G.
73. (NEW) A method of preparing the immunogenic composition of claim 72, said method comprising culturing a recombinant host organism transfected with an

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expression vector encoding, in an expressable form, the amino-terminal portion of the heavy chain of a botulinum neurotoxin serotype.

74. (NEW) A method of preparing the immunogenic composition of claim 72 comprising culturing a recombinant organism capable of expressing the amino-terminal portion of the heavy chain of a botulinum neurotoxin serotype and recovering an insoluble protein fraction from the recombinant organism.
75. (NEW) An immunogenic composition comprising at least a portion of the heavy chain of a botulinum neurotoxin serotype selected from the group consisting of serotype B, serotype C<sub>1</sub>, serotype D, serotype E, serotype F, and serotype G.
76. (NEW) The immunogenic composition of claim 75, wherein said portion of the heavy chain of a botulinum neurotoxin serotype elicits an ELISA response to the corresponding botulinum neurotoxin serotype in an animal, said ELISA response being detectable upon about 100-fold dilution of serum from said animal.
77. (NEW) The immunogenic composition of claim 75, wherein said portion of a botulinum neurotoxin serotype comprises at least one epitope of the amino-terminal portion or the carboxy-terminal portion of the heavy chain of a botulinum neurotoxin serotype selected from the group consisting of serotype B, serotype C<sub>1</sub>, serotype D, serotype E, serotype F, and serotype G, wherein said epitope is capable of eliciting protective immunity toward the corresponding botulinum neurotoxin serotype.

78. (NEW) The immunogenic composition of claim 77, wherein said immunogenic composition elicits an ELISA response to a botulinum neurotoxin serotype in an animal, said ELISA response being detectable upon about 100-fold dilution of serum from said animal.
79. (NEW) The immunogenic composition of claim 75, wherein said composition is endotoxin free.
80. (NEW) A nucleic acid encoding a protein comprising at least one epitope of the amino-terminal portion or the carboxy-terminal portion of the heavy chain of a botulinum neurotoxin serotype selected from the group consisting of serotype B, serotype C<sub>1</sub>, serotype D, serotype E, serotype F, and serotype G.
81. (NEW) The nucleic acid of claim 80, wherein said protein is a fusion protein further comprising a non-toxic polypeptide sequence.
82. (NEW) A recombinant host cell comprising the nucleic acid of claim 39, 57, or both.
83. (NEW) The recombinant host cell of claim 82, wherein said host cell expresses a protein comprising at least a portion of the heavy chain of a botulinum neurotoxin serotype selected from the group consisting of serotype B, serotype C<sub>1</sub>, serotype D, serotype E, serotype F, and serotype G.
84. (NEW) The recombinant host cell of claim 83, wherein said protein elicits an ELISA response to a botulinum neurotoxin serotype in an animal, said ELISA response being detectable upon about 100-fold dilution of serum from said animal.